UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF NEW YORK

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TEVA PHARMACEUTICALS USA, INC., TEVA PHARMACEUTICALS INDUSTRIES LTD., TEVA NEUROSCIENCE, INC. and YEDA RESEARCH AND DEVELOPMENT CO. LTD.,

Plaintiffs,

v. 08-CV-7611 (BSJ)

SANDOZ, INC., SANDOZ INTERNATIONAL GMBH, NOVARTIS AG, and MOMENTA PHARMACEUTICALS, INC.,

Defendants.

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TEVA PHARMACEUTICALS USA, INC., TEVA PHARMACEUTICALS INDUSTRIES LTD., TEVA NEUROSCIENCE, INC. and YEDA RESEARCH AND DEVELOPMENT CO. LTD.,

Plaintiffs,

v. 09-CV-8824 (BSJ)

MYLAN PHARMACEUTICALS INC., MYLAN INC., NATCO PHARMA LTD.,

Defendants. Non-Jury Trial

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New York, N.Y.
September 7, 2011
9:30 a.m.

Before:

HON. BARBARA S. JONES,

District Judge

APPEARANCES

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ALSO PRESENT: CORT CHASE, Litigation Support

(Case called)

(In open court)

THE COURT: Good morning. All right, I have some rulings for you this morning, and then I guess we can proceed with openings. Let me start with what we discussed first I think the last time we were together, which is Mylan's application that Teva be ordered to produce Mr. Konfino. I'm denying that. I've read the cases, particularly, I don't know how to pronounce the name, Minvea (ph). It just doesn't stand for the proposition that defendant is claiming it does. The judge didn't order the experts to show up for trial in the first instance, he basically said you can bring them or you can suffer an adverse inference. More importantly, it just doesn't stand for the proposition that if there is an agreement of the type that we have in this case, that there's any obligation on the part of the patent holder in this case, Teva, to produce the inventor for trial. Teva as a party who controls Mr. Konfino is certainly obligated to produce him for deposition. They have done that. I think that's the extent of their obligation.

All right.

MS. BLOODWORTH: Your Honor, if I may be heard after that as well.

THE COURT: I have read several letters, Ms. Bloodworth. What else is there to say?

MS. BLOODWORTH: To clarify your rulings, plaintiffs have also designated Mr. Konfino's deposition transcript. We believe it should be admissible under Rule 804, because if plaintiff had requested him to come here to trial, he testified in his deposition he would appear, and he's also added his contract doesn't make clear if he's actually obligated to Kenyon that he would appear.

THE COURT: I'm not sure that's not the same argument that you've been making. He's not within the subpoena power of this Court. Under that circumstance, his deposition testimony should be admissible. Mr. Hashmall?

MR. HASHMALL: Just one point of clarification. We did not designate his deposition testimony, we counter designated it in response to the designation made by Sandoz.

THE COURT: I see. So Sandoz is intending to offer it.

MR. HASHMALL: That's correct, and we did counter designate.

THE COURT: All right. Teva's move to prevent Sandoz from presenting its obviousness defense, I'm denying that motion. Look, I read the interrogatory responses, and they certainly weren't as specific or as clear as they could have been. However, they're clearly intending to identify obviousness as a defense in view of the '550 patent as a basis for invalidating the patents in suit. And I think I've read

some of Dr. Rice's testimony in addition to reading the quotes in Sandoz' letters, and certainly some of those facts were relevant to an obviousness analysis. And I don't believe Teva will suffer any prejudice from Sandoz' presentation of its obviousness defense. It's highlighted as serving the same defense.

Lastly, Mylan has made a motion in limine to preclude Teva from offering evidence of unexpected results over the course of prior art and I guess that having read it, the crux of the motion is that Teva's evidence is insufficient to establish unexpected results to overcome a prima facie case of obviousness. I don't know. I can't make that finding now through an in limine motion, I'm going to hear the evidence. After I do, then I can determine that particular question.

All right. Those are the three motions that I wanted to give you my rulings on.

Lastly, just in terms of scheduling, I read your letter. If the trial extends beyond September 23, because of the Jewish holidays, Rosh Hashana and my own availability, the trial will resume the week of October 3. I understand that's good for all the parties, is that right?

Is there any other housekeeping matter before we go forward?

MS. BLOODWORTH: Yes, your Honor. We have one more. We had submitted a pro hac vice application for David Jones, my

colleague from the Madison office and there's been no objection. I spoke with plaintiff's counsel and Sandoz counsel this morning and we request that be granted.

THE COURT: All right, I'll grant it right now.

MS. BLOODWORTH: Thank you.

THE COURT: Was it David Jones?

MR. JONES: Yes, your Honor.

THE COURT: Opening statements, then.

MR. DOYLE: Your Honor, if I could make one very brief statement for the record?

THE COURT: Sure, go ahead.

MR. DOYLE: Just relating to the claim construction order. For the record, your Honor, Sandoz' objection to the Court's claim construction needs to be noted and I'm noting it now and Sandoz does maintain that the claim constructions that it advocated are the correct claim constructions and I wanted to of course indicate Sandoz will apply the Court's claim constructions throughout the trial and we do ask the Court to consider all the evidence once it had heard all the evidence in connection with claim construction issues that are relevant to its ultimate findings of fact and conclusions of law.

Thank you, your Honor.

THE COURT: All right. Thank you, Mr. Doyle. Ms. Holland, are you going to begin?

MS. HOLLAND: Yes. Thank you, your Honor.

Good morning. Sandoz' and Mylan's defenses have been a moving target since the beginning of this case. At first Sandoz said its best defense was indefiniteness. In fact, it said it was such a strong defense that the case could be disposed of on summary judgment. When Sandoz' motion for summary judgment on indefiniteness was denied then inequitable conduct became its best defense and Mylan asked for an early trial on that issue.

THE COURT: Ms. Holland, I'm going to ask you to slow down a bit before the reporter does.

MS. HOLLAND: I'll move closer.

THE COURT: Okay, thank you.

MS. HOLLAND: So what remains here for trial, your Honor, are essentially defendant's third tier defenses. So what are we left with here? On infringement what remains after the Court's claim construction is Mylan's argument that it doesn't infringe because its product isn't copolymer-1 and as your Honor knows after three years of litigation Sandoz for the first time two weeks ago decided that its product also wasn't copolymer-1.

On invalidity, defendants can't even agree among themselves what their defenses should be. Mylan says that the claims are anticipated and obvious over the '550 patent. Sandoz doesn't make any kind of anticipation argument and it's obviousness argument was not even fleshed out until two weeks

ago. Sandoz, on the other hand, continues to argue here that the claims are indefinite because the patents in suit don't have the specific calibration standards that Teva used in its laboratory to do its SEC analysis and apparently Sandoz is no longer asserting that the conditions aren't stated would be a basis for indefiniteness. But Mylan in any event is no longer presenting this defense at all.

Both defendants say that the inventor, Mr. Konfino, had a best mode for removing an impurity or minimizing an impurity called bromotyrosine and that this best mode didn't appear in the patent, but, again, defendants can't even agree on what Mr. Konfino's best mode was and the evidence is going to show that their best mode arguments are actually inconsistent with each other.

In any event, whatever their best mode is it's not anything that has to do with Mr. Konfino as we have here. Was a manufacturing specification. It has to do with the commercial product. Mr. Konfino was a bench chemist working in his laboratory. He didn't set any kind of specification for bromotyrosine. You're also not going to hear a single expert get up on the stand and say this bromotyrosine impurity has any effect on efficacy, or on safety of copolymer-1. It just doesn't make any difference in the product.

What I'd like to do for the next couple of minutes is just to focus in on a couple of these defenses in a little more

detail. Let me start first with infringement. As I said earlier, based on the Court's claim construction defendants aren't contesting that their products meet almost all of the limitations of the asserted claims, including the average molecular weight limitations. Since defendants, your Honor, have refused to enter into a stipulation on this, we're going to be spending the next couple of days presenting evidence that shows that the Sandoz product and Mylan product meet each and every limitation of the asserted claims. So the only non-infringement defense that Mylan continues to press here is that its product isn't copolymer-1 because it doesn't have the right molar ratio. The fact that this is a completely litigation-driven argument, your Honor, becomes very evident when we look at what Mylan told the FDA in its FDA filings outside the context of this litigation. So what we have here, your Honor, is from Mylan's ANDA and as you can see the formal name for its actual ingredient is called glatiramer acetate, that's the active ingredient in Copaxone as well, but Mylan told the FDA that another name for the active ingredient is copolymer-1.

And what's really important to focus in on here, your Honor, is at the bottom where it shows the average molar fractions. The average molar fractions represent the percentages of the four amino acids in the product and this is the information you use to get to the molar ratios. These are

the exact same molar fractions that you're going to hear Mylan tell you mean that its product is not copolymer-1. But when it spoke to the FDA, Mylan said these very same molar fractions, this very same product is copolymer-1. Now, remember, your honor, Sandoz never even made this argument until two weeks ago. For the first two years of this litigation Sandoz acknowledged as it had to that its product was copolymer-1 and if we look again at how Sandoz characterized its product outside the context of this litigation we'll see why it never asserted it wasn't copolymer-1.

This is from a 2005 internal report from Momenta, and Momenta is Sandoz' partner in its generic product. As you can see here again, what Momenta and Sandoz are saying is the active ingredient in its product is copolymer-1 and again shows the molar fractions, the percentages of these of these four amino acids in its product. These are the same molar fractions you're going to be hearing about during the course of this case. These are the same molar fractions, your Honor, that appeared in the July 2011 briefing book that we discussed at the pretrial conference. So what this shows, your Honor, is that Sandoz understood that these molar fractions, molar ratios of its product meant that its product was copolymer-1 and as I said at the pretrial conference, bringing this up at the last minute based on this July 2011 briefing book, it was just a pretext to get this defense into the case.

Now, your Honor, we've been discussing this term molar ratio at a lot of the pretrial conferences, so I think we should spend some time discussing exactly what that is and why the Mylan and Sandoz products meet the molar ratios of the claims.

So just to go back for a minute, copolymer-1 is a mixture, of polypeptides, different chains of different lengths but all these chains contain these four amino acids that are listed here; alanine, glutamic acid, lysine and tyrosine. In any copolymer-1 mixture those are going to be the four amino acids that appear in the polypeptide chain, a chain of different lengths, different sequences, but those are the four that appear.

When we talk about the molar ratio, what we mean are the ratios of these four amino acids in the mixture, and molar ratio refers to the ratio of moles, which is just a unit of measurement that chemists use, but it's the relevant proportion of these four amino acids in the mixture. So when the claim requires a molar ratio of approximately 6:2:5:1, what it means is that any copolymer-1 mixture is going to have these four amino acids in approximately this relative proportion to each other, six alanine to two glutamic acid to five lysine to one tyrosine, and that's going to be any copolymer-1 mixture, approximately that ratio.

Now, I think the best way to illustrate this is to

think about a single polypeptide chain in the copolymer-1 mixture and what I have here on the screen is a chain of 14 amino acids and that's probably the most convenient way to look at this, because the molar ratio is 6:2:5:1, and if you add that up it comes out to 14. So for illustrative purposes it's easier to look at it this way. So in this chain of 14 amino acids, six of the 14 would be alanine, so that's approximately 43 percent; two of the 14 would be glutamic acid, approximately 14 percent; five of the 14 would be lysine, approximately 36 percent; and one of the 14 would be tyrosine, approximately 7 percent. So really, your Honor, this is the crux here of the molar ratio and what it means.

If you look at a sample, the question we're asking here for molar ratio is does this sample have approximately 43 percent alanine, 14 percent glutamic acid, 36 percent lysine and 2 percent tyrosine. That would go for any copolymer-1 mixture any length of chain.

So you can apply the same thing to a chain, for example, of 70 amino acids, and the reason I chose 70 here, your Honor, is because that would be the length of chain of amino acids for a copolymer-1 polypeptide that was about 7.5 kilodaltons, kind of in the middle of the five to nine kilodalton range. If you think about an average length of chain of a polypeptide in copolymer-1 it would be 30 out of 70 or 43 percent alanine, 10 out of 70 or 10 percent glutamic

acid, 25 out of 70 or 36 percent lysine and five out of 70 or approximately 7 percent tyrosine. That's the fundamental concept.

We have to determine the ratios or the proportion of these four amino acids as part of the total copolymer-1 mixture. So let's apply this now to the Mylan and Sandoz products.

So let's talk about Mylan first. Your Honor, I showed you those molar fractions in the ANDA and this comes out of Mylan's ANDA. These are the molar fractions Mylan tells the FDA it has in its product; .427 alanine, .144 glutamic acid, .336 lysine, and .092 tyrosine. If you express those as percentages, as I did on the previous slides, it's approximately 43 percent alanine, 14 percent glutamic acid, 34 percent lysine and 9 percent tyrosine. That's what Mylan's product is. When you compare that to exactly 6:2:5:1 that I showed on the slide earlier, you see the alanine/glutamic acid spot on exact same percentages. The only difference is in lysine, the tyrosine. 2 percent less lysine, 2 percent more tyrosine. Your Honor, this is well within what any of the experts in this case, 2 percent or 4 percent total would say falls within approximately 6:2:5:1.

And it's the same thing for the Sandoz product, your Honor. The molar fractions that I have here on the screen come from the July 2011 briefing book. But we see the same thing.

Alanine/glutamic acid, same percentages as exactly 6:2:5:1. Only difference is 2 percent less lysine 2 percent more tyrosine, again well within what any expert or anyone in skilled in the art would consider to be approximately 6:2:5:1.

And if you just think about this again in the context of what are we actually talking about, what does this 2 percent actually mean in a copolymer-1 polypeptide, let's go back to the 70 amino acid polypeptide we discussed earlier. And this 2 percent difference in lysine and tyrosine, your Honor, in a 70 amino acid chain, an average chain, would amount to one more tyrosine out of 70 amino acids and one less lysine, your Honor. That's it. That's the difference between the products of Mylan and Sandoz and exactly 6:2:5:1. This is what defendants say makes their product not copolymer-1.

I want to talk for a moment about an argument that Mylan makes. They say you have to do a mathematical manipulation called normalizing to tyrosine before you compare their molar ratios to 6:2:5:1. You see on the screen normalizing means essentially fixing the values of one of the amino acids and comparing the other three to the fixed values so you're not looking any more at the percentage of the total mixture, you're looking at the percentages of, in the case of tyrosine, for example, alanine, glutamic acid and lysine a compared to tyrosine, so the numbers come out a little different for that reason.

First of all, your Honor, there's nothing whatsoever in the patent about normalizing for tyrosine. It's not there at all. But what's really important is that normalizing the tyrosine is really just a different way of displaying these molar fraction percentages. It doesn't change the conclusion of the percentages of each of these four amino acids in the copolymer-1 position. So, for example, if you look at product normalized to tyrosine, you'll see that the total scale on the bottom is 10.86. So if you add up the 4.64, 1.57, 3.65 and 1, you get to 10.86.

Before we were looking at it on a scale of 14, now it's 10.86. But if you take the percentages of each of those amino acids out of 10.86, your Honor, you see it's the exact same percentages we saw earlier. Normalizing to tyrosine, it cant's change what's actually in the mixture. It's just a different way of looking at the numbers. And if you normalize to tyrosine and look at it on the same scale you get the same answer. The only difference is in the lysine and tyrosine, that 2 percent.

Now, Mylan normalizes to tyrosine because if you look at the numbers it makes it look like it's the biggest difference in numbers from 6:2:5:1, but you can actually normalize any of the formula because all it means is the fixing of the values. Again, your Honor, if you do the math you'll see they're all on a different scale if you normalize, but if

you do the percentages based on the right scale for each of these normalized numbers you get the same answer. Any way you look at it, your Honor, the percentages of the four amino acids in the mixture, the only difference from exactly 6:2:5:1 for the products in this case is this small 2 percent difference in lysine and tyrosine.

I want to turn next to Sandoz products that the patents are indefinite or not enabled because again they don't disclose the exact calibration standards that Teva used in its laboratory to conduct this analysis. And this, of course, is the same issue that Sandoz and Mylan raised in their summary judgment motions and, again, Mylan isn't even making this argument anymore. But there's nothing new here, your Honor. According to its pretrial brief what Sandoz is going to be arguing is the same thing it argued before, that it had a lot of trouble developing a generic Copaxone product and this somehow indicates the patent wasn't enabled. But what is at issue here, your Honor, is whether a person of ordinary skill in the art can figure out whether a sample of copolymer-1 fell within the weight limitations. That's it. Mylan and Sandoz are not making this argument anymore. They actually had no trouble figuring out how to determine the molecular weight of the copolymer 1 sample.

This is from a document that Mylan submitted to the FDA in responses to Teva's submissions and what Mylan said to

the FDA was there are testing methods, testing systems that you can use to determine the average molecular weight ranges of a copolymer-1 sample and that these could be easily employed for any generic version of Copaxone. So Mylan understood that it's not hard to determine the average molecular weight of a copolymer-1 sample. These are easy testing methods that could be input for any generic version of Copaxone. In fact, your Honor, Mylan actually used universal calibration, which is a technique that Sandoz says can't be used to figure out accurately the molecular weight of copolymer-1, but Mylan did use universal calibrations and submitted the results to the FDA.

You're also not going to hear at trial from defendants or Sandoz expert Dr. Svek. Now, you may recall Dr. Svek from the claim construction stage, your Honor. He was Sandoz' expert at the claim construction stage, but he wasn't invited by Sandoz to come to trial here. And if you look at what he said at his deposition it's not hard to figure out why you won't be seeing him live. This is from Dr. Svek's October 2009 deposition. This is part of the designated deposition testimony in this case. Dr. Svek was asked in his deposition, "In 1994 if someone has given you a sample of copolymer-1 would you have been able to determine whether it had a molecular weight between 5,000 and 9,000" -- it should say daltons it says kilodaltons.

And he said, "Probably yes, yes." Exactly the opposite of what Sandoz is going to be arguing to the Court here during this trial.

It's also important to understand that what Sandoz and Momenta have to do to establish for FDA purposes that their generic product is the same as Copaxone is an entirely different analysis than what we're doing here in this courtroom because what is important here only is whether a person of ordinary skill in the art would be able to determine whether a copolymer-1 sample fell within the molecular weight limitations of the claims.

Now, I have a slide I want to use, your Honor, but I think it's only going to come out on our private screens because I understand there's a confidentiality issue.

THE COURT: Okay.

MS. HOLLAND: For patent purposes your Honor, and the argument that Sandoz is making here, that the molecular weight limitation is enabled, a person with ordinary skill in the art could figure out whether it meets that limitation. But what we have here on the right, your Honor, is a listing of only some of the tests that Sandoz had to do in order to get its ANDA on file. They had to perform dozens and dozens of analyses of all different kinds of characteristics of its product and compare them to Copaxone, all different kinds of parameters that had nothing to do with molecular weight. They did have to do a

molecular weight determination, but that was a very small fraction of what had to be done by Sandoz in order to develop its generic Copaxone products so evidence of what Sandoz had to do to try to develop a generic Copaxone product doesn't have any relevance to whether or not a person of ordinary skill in 1994 would have been able to determine whether a copolymer-1 sample fell within the molecular weight limitations.

Just as the final point, your Honor, the primary prior art references that are going to be referred to that were relied on here by defendants for their anticipation and obviousness arguments are the '550 patent and the 620 EP publication. Both of those references were thoroughly considered by the Patent Office over years and years of prosecution and the Patent Office decided that the patent claims were not obvious, they were not anticipated for either of those references. So as the federal circuit has told us in that kind of situation defendant's burden here is even higher than it ordinarily would be. And, your Honor, the evidence is going to show there's no reason for the Court to come to any different conclusion than the one that was reached by the Patent Office.

In sum, your Honor, the evidence is going to show that the Mylan and Sandoz products here are of course copolymer-1 and they meet all the other claim limitations and defendant will not be able to meet their burden by proving by clear and

convincing evidence that any of the patent claims asserted here are invalid. Thank you.

THE COURT: Thank you, Ms. Holland. Ms. Bloodworth?

MS. BLOODWORTH: Yes, your Honor. Thank you, your Honor. The court reporter is ready? My name is Shannon Bloodworth and I'm going to speak on behalf of the Mylar codefendants. What I'm going to spend my time focusing on is a critical point of distinction between Copaxone and the Weizmann copolymer-1. Simply put, Mylan will show that the copolymer-1 that is described in the patents in suit, is not the copolymer-1 product that Teva disclosed to the FDA for approval to market as Copaxone and is not the same as Mylan's product. Rather, the patents in suit cover an old composition of copolymer-1 dating back to the early 1970's. To be sure, Teva alleges that the patents in suit disclose copolymer-1 having a slightly lower molecular weight than the old copolymer-1, but the composition of the old copolymer-1 disclosed in the patents in suit in the 1970's are the same, and they share essentially the same molar ratio.

This ratio in the '808 patent, as you heard Ms. Holland say is approximately 6:2:5:1. What this means is there's a chemical composition of copolymer-1 where there are six alanines for every two glutamic acids for every five lysines for every one tyrosine. As I'll explain, this 6:2:5:1 ratio differs substantially from the ratios in Copaxone and in

Mylan's proposed glatiramer acetate product, and this substantial difference in the molar ratio is why Mylan's patent does not infringe on the patents in suit.

So why is there a difference? The patents in suit disclose a process for making copolymer-1 that result in a thick and unwanted amino acid called bromotyrosine. By contrast, Copaxone, in Teva's own words, is significantly improved.

In the summer of 1989, a Teva scientist by the name of Mr. Eliezer Konfino identified bromotyrosine. And Mr. Konfino determined that bromotyrosine is formed during the second step in the copolymer-1 synthesis, when the free bromine present during the HBr or hydrobromic acid in acidic acid solutions bonds with approximately 30 percent of the tyrosine amino acids in the copolymer-1 polypeptide chains. So the free bromine is present in HBr acidic acid solution, bind with tyrosine approximately 30 percent of the time to form bromotyrosine. This doesn't happen one time with one 70 amino acid polypeptide chains. There are millions of chains in copolymer-1. This bond irreversibly converts those tyrosines to bromotyrosine, the fifth amino acid.

So Mr. Konfino experimented to find a way to prevent bromotyrosine from forming during copolymer-1 synthesis. His solution uses a chemical called phenol to scavenge the free bromine in the HBr acidic acid solution to prevent the

formation of bromotyrosine. So the phenol is used with the solution and it will bond with the bromines so they are no longer free to bond with the tyrosines in the copolymer-1 chain. The result, a form of copolymer-1 largely free of bromotyrosine and without about 30 percent more tyrosine than that found in the old form of copolymer-1.

Now, there's a 30 percent, about 30 percent more tyrosine because almost none of it is converted to bromotyrosine thanks to the use of phenol. The new form, the free of bromotyrosine form, is what is marketed as Copaxone. It has a molar ratio of 4.5 alanine to 1.5 glutamic acid to 3.6 lysine for every one tyrosine. Now, the Copaxone molar ratio is not approximately 6:2:5:1 just disclosed in the patents in suit and that's because is more tyrosine in Copaxone than in the old form of copolymer-1. And because there is more tyrosine, the other three amino acids are reduced. That's the essence of a ratio. They're different compositions and they have different molar ratios.

Mylan, like Teva, uses phenol to produce its glatiramer acetate. Consequently, Mylan's product like Copaxone, is substantially free of bromotyrosine and has a molar ratio of approximately 4.6 alanine, 1.6 glutamic acid, 3.7 lysine for every one tyrosine. And you will hear testimony from Mylan's expert, Dr. Steven Kent, who will explain that the Mylan molar ratio is not approximately 6:2:5:1. The Mylan

product has a fundamentally different composition than the copolymer-1 claimed in the patents in suit, and this means that the Mylan product does not infringe any of the patents in suit which all define copolymer-1 as having a ratio of approximately 6:2:5:1.

Now, as you heard a little bit in the beginning in the opening from Ms. Holland, Teva will try to downplay the importance of this new form of copolymer-1 or Copaxone,and Mr. Konfino's process for making it, but the science and Teva's documents tell a very different story. For example, an internal document apparently used phenol to rid copolymer-1 of the bromotyrosine is a, quote, a major improvement in the production process, and Mr. Konfino himself declared the use of phenol to be the, quote, most convenient process for synthesizing low bromotyrosine cop-1. Indeed, the virtue of Mr. Konfino's discovery was quickly recognized by Teva and by December 1989 Mr. Konfino's boss, Dr. Lenol approved a new Teva manufacturing protocol that incorporated Mr. Konfino's phenol process. And later when Teva applied for an approval to market Copaxone, Teva disclosed this improved form of copolymer-1 and the use of phenol for making it in a confidential submission to the FDA. To this day Teva makes the improved form of copolymer-1, manufactured using phenol and sells it as Copaxone.

Now, the evidence will further show that prior to this

litigation when plaintiffs calculated the molar ratio Copaxone, they did so in the same manner that Dr. Kent will explain. For instance, Yeda, Teva's partner and coplaintiff in this case obtained the '287 patent in 2004. This patent is not asserted here, your Honor, but it is known as the Gad patent under the first named inventor Dr. Gad. In this patent it claims or it describes the molar fractions of glatiramer acetate to be .427 alanine, .141 for glutamic acid, .337 for lysine and .098 for tyrosine. The molar fractions are the underlying data used to calculate the molar ratios, and the Gad patent also defines the molar ratio for glatiramer acetate as approximately 4.6 to 1.5 to 3.6 to 1. If there's no material difference in approximately 6:2:5:1 to the molar ratio recorded in the Gad patent for glatiramer acetate, then why here is it reported as approximately 6:2:5:1? The answer is because they are different. They describe very different copolymer-1 compositions.

And, interestingly, Dr. Gad also calculated the molar ratio in the same way that Dr. Kent did. Dr. Gad divided by the least abundant amino molar fraction, tyrosine, and he divided across the four amino acids and you get the molar ratio of 4.6 to 1.5 to 3.6 to 1. The result is a molar ratio indistinguishable from Mylan's and Copaxone's molar ratio.

Now, according to Ms. Holland, Mylan has erred in the way we calculated the molar ratio. But as we just saw in the

Gad patent, Mylan's calculations of the molar ratio are the same way that Yeda reported the molar ratios in the Gad patent. But even using Teva's expert method to calculate the molar ratio where you add up 6:2:5:1 and multiply by 14, you'll still see a 30 percent, about 30 percent difference in the tyrosines. I don't have Ms. Holland's slides, but you'll recall that one of the numbers was 1.29 for tyrosine, one was a 1.33, I believe, that's about a 30 percent difference between 1. And Teva's expert gets rid of this extra tyrosine by rounding it down to one. As Dr. Kent will explain, rounding has no place in a field characterized by precision, particularly when doing so obscures an approximately 30 percent difference between the old copolymer-1 and the composition known as Copaxone.

Interestingly enough, Teva did also eventually patent its phenol process in 2009, in the '072 patent or also what we call the Dolitzky patent after the first named inventor. Teva has also not asserted this patent in this litigation. But the Dolitzky patent is important for two reasons. First, it shows that Teva believed the use of phenol to obtain low bromotyrosine cop-1 was an improvement worthy of additional patent protection. Secondly, the '072 patent has approximately the same molar fractions that were reported in the Gad patent and he used the same normalization calculation as did Mylan, as did the Gad patent. You'll see that the molar ratios are once again substantially different.

So again, we'll see the molar ratio in the Dolitzky patent of Teva's, the Gad patent in Yeda and the normalization calculations are all substantially different and much different than the approximately 6:2:5:1 in the patents.

But Copaxone which was made using the phenol to eliminate or substantially reduce the presence of bromotyrosine is not described in the patents. In fact, neither phenol nor bromotyrosine is mentioned at all anywhere in the patents in suit. In the patents in suit Teva omitted the impact that the use of phenol had on the molar ratio of Copaxone choosing instead to report the old copolymer-1 ratio of 6:2:5:1. Teva has to prove today by a preponderance of the evidence that Mylan's glatiramer acetate is what is claimed in the patents in suit. It's not enough to say Mylan's glatiramer acetate was the same as Copaxone. It's not the proper legal comparison. So the comparison that must be made, therefore, is between Mylan's proposed glatiramer acetate product and the claims of the patents in suit. All that's required is approximately 6:2:5:1, and when this comparison is made it is claimed that the Mylan product, like Copaxone made with phenol to reduce bromotyrosine simply does not fall within the ratio disclosed in the patents.

Finally, in the invalidity portion of the trial the evidence will show that Teva failed to disclose its use of phenol to achieve low bromotyrosine cop-1. The evidence will

show, particularly through the testimony of Dr. Alan Zeiger that nothing was added by the '808 patent to the process of what was invented at the Weizmann Institute and claimed in 1974 in the '550 patent. All Teva did was disclose and use obvious steps pertaining to the art to purify the Weizmann copolymer-1 to a molecular weight that still overlapped with the '550 patent. In short, Dr. Zeiger will explain that Teva simply patented an old process with only obviousness modifications.

Thank you, your Honor.

THE COURT: Thank you Ms. Bloodworth. Mr. Doyle.

MR. DOYLE: Your Honor, Ms. Hagberg will be presenting the opening for Sandoz.

THE COURT: All right.

MR. HAGBERG: Your Honor, my first challenge is getting to the podium.

MS. HOLLAND: Your Honor, is this the same thing that's on the screen?

MR. HAGBERG: We'll be moving back and forth. There isn't any other space in the courtroom.

THE COURT: I think maybe you can move it back. I'll be able to see and counsel can stand there.

MR. HAGBERG: Good morning, your Honor. I think this is the first time I've spoken here in this case. As Mr. Doyle said, I'm Karen Hagberg. I'm from the New York office of Morrison Foster.

Your Honor, I'm going to be focusing on enablement here today, which contrary to what Ms. Holland said it's neither a new defense nor is it by any means a third tier defense of Sandoz and Momenta. As your Honor knows from the inequitable conduct portion of this trial, the path of this dispute to the courtroom this morning has been a very, very long one, and as Dr. Arnon testified, that path started about 40 years ago and that's why we have this time line, your Honor, is just to show how long it took for Teva to get to the position that it's at today.

Dr. Arnon's work started 40 years ago at the Weizmann Institute when they first formulated and began experimenting with copolymer-1. That work resulted in the '550 patent which we have up there on the time line and the application was filed in 1971 and the patent issued in 1974. And at the time of that filing, what did Teva represent? It noted that copolymers according to the present invention are easily prepared by conventional procedures. 20 years later in 1994, the next date on the time line, in its first filing related to the patents that are at suit here, Teva repeated basically the same representation that it told the Patent Office in 1971. Copolymer-1, according to the present invention, may be prepared by methods known in the art. For example, the process disclosed in the '550 patent. In other words, what Teva has consistently told the Patent Office over the last 30 years is

that copolymer-1 is prepared merely by following methods known in the art, but these statements in the '550 patent and present in all the patents that are at issue here today contrast dramatically with the testimony of Dr. Pinchasi that you heard in July.

In July Dr. Pinchasi could not have been clearer. One of the two strategies that Teva depended on in order to avoid competition from generic producers of copolymer-1 was the difficulty that Teva had experienced in producing its product, and she basically said that we realized very quickly when we started to experiment with the substance that it's absolutely not a simple product and it's not easily reproducible, so we felt this by itself is going to constitute a relatively high level of entrance for generic companies.

The evidence in this case will confirm that that was indeed the strategy that Teva followed, and that Dr. Pinchasi's July testimony in this regard is absolutely correct. The evidence will show that Teva itself spent many, many difficult years experimenting and learning how to measure the molecular weight of copolymer-1. And the evidence will also show that Teva kept critical aspects of the knowledge that it gained over all those years to itself. Teva did not, as the law requires, disclose in its patent how one skilled in the art could determine the copolymer-1 that it was producing had the same molecular weight as is required by the patent claims. And I

put the enablement statute up here just to make clear that what's required of the patent holder is that the specification must contain a written description of the invention in such clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and the evidence will show that exactly is what Teva did not do.

Now, as your Honor knows, enablement speaks to the person of ordinary skill in the art at the time of filing of the patent application, which here is 1995, and there's been some dispute about what would be known and what wouldn't be known, but in this case, your Honor doesn't have to decide enablement just based on what experts are saying in 2011 about what persons of skill in the art would know or would have done in 1994. Sandoz will present evidence of what the scientists at the Weizmann Institute and at Teva did and knew in the dozen years leading up to the 1998 disclosure of the standards that they finally decided on after their many, many years of experimentation.

There can be no dispute that these scientists were at least persons of ordinary skill in the art at the relevant time period. There can also be no dispute that contrary to Ms. Holland's argument today that it was easy, that it took these scientists years of experimentation between 1986 and 1998 to determine how to accurately and reproducibly measure the molecular weight of copolymer-1. And if I may, your Honor, we

have a second time line that's just focused on the molecular weight aspects of the development of copolymer-1. So we start with 1986, and in those days Teva is using the method that the Weizmann Institute had been using. As Dr. Arnon confirmed in her testimony in July the method is ultracentrifugation and the resulting measurement is weight average molecular weight. By 1987 Teva had switched to size exclusion chromatography, what is referred as SEC, actually your Honor, just because I found this interesting, I don't know whether you've ever seen it this is actually the Superose 12 SEC tube that is used to measure and that is talked about in the patent. And by the way, this is really all that the patent discloses is the column and its filled with the Superose beads. There's nothing in the patent about the disclosure of the standards that Teva chose in 1994 and 1995 to calibrate that column.

So throughout 1987 and 1988, Teva has difficulty picking the standards to provide an accurate molecular weight measurement for copolymer-1. First it attempts to use commercially available globular protein standards, but then it learns that SEC with these standards produce molecular weight measurements that are vastly higher than the weight measurements that were provided by other techniques that they could provide. In fact as Teva's test results show, the measurements were at least four to six times higher than molecular weights determined by viscosity and

ultracentrifugation.

So in 1988 Teva uses another set of commercially available standards, polyethylene glycol, to calibrate the columns for the molecular weight analysis and they subsequently abandon that approach as well.

Later that same year in 1988, Teva's consultant attempts to determine absolute molecular weight of copolymer-1 using a technique called osmometry, and they're expecting to see a value of 7,000 daltons based on prior characterizations. But what do they get? The osmometry result is only 638 daltons which is more than tenfold less than the value that they had obtained by other methods in tests on the same copolymer-1 batch.

Now, still within this 1987-1998 time frame, Teva begins to experiment with the use of copolymer-1 self standards and it applies a set of calculations to correlate the molecular weight from viscometry with results from SEC. It continues with this viscometry correlation procedure until 1992 when it sets forth a new protocol for its molecular weight calibration. The new calibration uses as standards which are referred to in markers in the Teva documents, Teva's own batches of copolymer-1 whose molecular weights have been characterized by yet another method, moles. The evidence will show in 1994 Teva continues to measure molecular weight with this proprietary molecular weight cell standard. Then in 1995 the FDA steps in

and it requests that Teva again tries to use commercially available SEC standards, and the FDA does so as stated in this document from Teva's own files that they want to insure that the molecular weight calibrations can be performed in any laboratory not relying on a single source for markers, and again, markers refers to standards.

And Teva does try, it tries to find a commercially available standard, but then it gives up and it reconfirms that the use of commercially available markers to generate calibration curves that accurately reflect the molecular weight of copolymer-1 is not feasible.

By now we're up to November of 1995, by the way. So then what does Teva do? In early 1996, it returns to its earlier position that the best markers for calibration of the SEC columns are copolymer-1 batches with a known molecular weight, in other words we're back to self standards. In 1996 Teva is also attempting to determine the molecular weight of copolymer-1 by another method, multitop, which is a type of spectrometry. That molecular weight results in far lower than even the broad range of values that were determined by the three other methods for the very same sample.

So what do they conclude? They conclude that the differences are due to the experimental bias of the technique and how data are calculated and presented, and they say themselves, therefore, it should be explicitly stated by which

analytical method the molecular weight data were obtained. In 1998 Teva reports to the FDA again that it's changing its analytical method for determining molecular weight and it switches its calibration standards from self standards, which the FDA wasn't in favor of, to synthetic peptide standards, which finally addresses the FDA concerns over the validity of self standards as calibration standards. And, by the way, those peptide standards are the basis of the Gad patent which issued starting in 2003 and which Teva has asserted in a separate lawsuit pending before your Honor. So despite all of this experimentation over so many years Teva did not disclose its preferred standards. In fact, it didn't disclose any standards for that matter in the patents that are in suit in this case.

The evidence will show that Teva's answers in '94-'95 to the difficulty of measuring copolymer-1's molecular weight, the use of self standards, creates an insoluble problem for persons of skill in the art. Because even assuming that persons skilled in the art eventually could develop copolymer-1 self standards, the lack of agreement among the methods for independently determining the molecular weight of those standards, it would preclude a person skilled in the art from developing the same calibration curve developed by Teva to produce the copolymer-1 that's claimed in the patents. And why is that? As your Honor will hear over the course of the trial,

the methods for producing and characterizing Teva's self standards are not disclosed in the patents, and persons of skill in the art would not know which method to choose to characterize molecular weights of their own self standards.

As I discussed a few minutes ago, different methods can give very different results and Teva knew that its use of self standards and the way to measure those standards should be explicitly stated. You'll also hear testimony from Sandoz and Momenta as well regarding problems they encountered in trying to arrive at molecular weight characteristics that are described in the commercially packaged Copaxone materials.

So I'd like to return to a point that I started with and that is from Dr. Pinchasi's testimony from the prior trial. Teva's strategy to keep competitors out was to rely on the difficulty of producing copolymer-1 and that difficulty you can see from the time line in how long it took them to get there. Teva has aggressively implemented that strategy to preclude generic competition including, as the evidence will show, by failing to disclose sufficiently enabling data in its patents and that strategy continues today. Between 2008 and 2010 Teva filed three citizen petitions with the FDA seeking to prevent FDA approval of the Sandoz ANDA and in its three petitions Teva has told the FDA what you'll hear from Sandoz' experts during the trial, that copolymer-1 is so complex that knowing you have the same molecular weight distribution in separate copolymer-1

comparisons is essential.

(Continued next page)

MS. HAGBERG: As Teva tried to persuade the FDA even the most minor changes in manufacturing will produce a new molecular entity with a significantly different potency and safety and efficacy policy.

The evidence at this trial will prove conclusively that a person of skill in the art must know the SEC standards to have any confidence that it is producing co-polymer-1 having the same molecular weight as what Teva claims it invented. And that is the information that is missing from the patents. Without that entablement, each of the patents is rendered invalid.

Thank you for your time this morning, your Honor, and to allow me to emphasize an area of the evidence that Sandoz and Momenta believe will be very critical to this case

THE COURT: Thank you, Ms. Hagberg.

All right. I don't think -- do I have a list of witnesses yet?

MS. HOLLAND: Yes, your Honor I believe we did send one, a list of witnesses. Do we have one -- we can get you a copy of that, your Honor.

THE COURT: Okay, I'm sure it came in. We just didn't see it.

MS. HOLLAND: Yeah, we'll find one.

THE COURT: All right. Then are you ready to proceed?

MS. HOLLAND: Yes. Mr. Hashmall is going to be

presenting our first witness.

THE COURT: Mr. Hashmall.

MR. HASHMALL: Good morning, your Honor. Plaintiffs would call as our first witness Mr. John Congleton.

JOHN CONGLETON,

called as a witness by the plaintiff,

having been duly sworn, testified as follows:

DIRECT EXAMINATION

BY MR. HASHMALL:

THE COURT: Take your seat, and spell your last name -- state your full name and spell your last name for the record.

THE WITNESS: John Congleton, C-O-N-G-L-E-T-O-N.

MR. HASHMALL: May I proceed, your Honor?

THE COURT: You may proceed.

MR. HASHMALL: Thank you.

Q. Good morning.

A. Good morning.

Q. Mr. Congleton, could you please introduce yourself to the Court?

A. Yes. My name is John Congleton. I'm senior vice-president and general manager for Teva Neuroscience.

Q. Could you tell us a little bit about Teva Neuroscience, its business?

A. Yes. Teva Neuroscience is focused on the commercialization

of Copaxone, as well Azilect for Teva in the United States.
Q. Where is Teva Neuroscience located?
A. It's located in Kansas City, Missouri.
Q. Approximately, how many people does Teva Neuroscience currently employ?
A. Approximately 600.
Q. When was Teva Neuroscience founded?
A. Teva Neuroscience was founded in 1995.
Q. Now, what is the relationship between Teva Neuroscience and the plaintiff in this action, Teva Pharmaceutical Industries?
A. Teva Neuroscience is a subsidiary of Teva Pharmaceutical Industries.
Q. And you know when Teva Pharmaceutical Industries was founded?
A. In 1901.
Q. You mentioned that Teva Neuroscience is in the business of selling Teva's branded products, is that correct?
A. Yes.
Q. Does Teva also sell, Teva Pharmaceuticals also sell generic products?
A. Yes, it does.
Q. Do you know overall for Teva's business approximately how much of its sales derives from generic products and how much derives from branded products?
A. Approximately 70 percent is from generics, and

approximately 30 percent is from brand pharmaceuticals.
Q. Now, you testified that you currently, you are currently senior vice-president and general manager of Teva Neuroscience. Could you briefly describe for the Court what your responsibilities are in that position?
A. Yes. I'm accountable for the sales and profits of the products that Teva Neuroscience commercializes, Copaxone and Azilect.
Q. Approximately, how many people report to you currently, Mr. Congleton?
A. Approximately 450.
Q. And how long have you been employed by Teva Neuroscience?
A. A little over 15 years.
Q. Could you briefly describe your educational and professional background prior to you joining Teva Neuroscience?
A. Yes. I have a bachelors degree in marketing from Kansas State University, started off in field sales in pharmaceuticals developmental roles, field sales manager position prior to joining Teva Neuroscience.
Q. Could you tell us a little bit about your employment prior to joining Teva Neuroscience?
A. That's the pharmaceutical sales rep, developmental role, human resource in field base sales manager.
Q. Do you have any degree in chemistry or biology?
A. No, I do not.

Q. Now, since joining Teva Neuroscience, what positions have you held at the company?
A. I have been a field sales manager, a product manager and a marketing department, the product director for Copaxone, general manager for our Canadian Division of Teva Neuroscience, as well as my current position, general manager for the United States division.
Q. Prior to you taking on your current position, could you just generally describe what your responsibilities have been with respect to Copaxone?
A. Yes. I started off as a product manager prelaunch preparing that product, and moved into the director of marketing for Copaxone as well.
Q. And do you continue to have responsibilities currently with respect to Copaxone?
A. Yes. It's under my span of control.
Q. Could you just generally describe for the Court what those responsibilities include?
A. Generally it's around the development and approval of our work plan, the budget, the resources we apply against the product, as well as strategic oversight.
Q. Now, you mentioned that in addition to Copaxone, Teva Neuroscience also sells markets, a product known as Azilect? Could you just briefly describe for the Court what Azilect is?
A. Yes. Azilect is a medication indicated for the treatment

both early, as well as ajunctive for ideopathic Parkinson's disease.

Q. Now, do you have a binder in front of you, Mr. Congleton with some documents in it?

A. Yes, I do.

Q. If you could, sir, just turn to the first tab, it's labeled as PTX 697. Do you see that?

A. Yes, I do.

Q. And have you seen this document before?

A. Yes, I have.

Q. What is it?

A. It is the prescribing information for Copaxone.

Q. Is this sometimes referred to as a product insert?

A. Yes.

Q. Is it also known as a drug label?

A. Yes, it is.

Q. Now, was this drug label for Copaxone approved by the Food and Drug Administration?

A. Yes, it was.

Q. Is this a document that was created and maintained by Teva in the ordinary course of its business?

A. Yes, it was.

MR. HASHMALL: Your Honor, plaintiffs move PTX-697 into evidence.

MR. JONES: No objection, your Honor.

MR. DOYLE: No objection.

THE COURT: All right, admitted.

(Plaintiff's Exhibit PTX-697 received in evidence)

Q. Mr. Congleton, what is the purpose of the product insert, which is PTX-697?

A. It's to describe the use, the efficacy, safety, ability of the medicine.

Q. Now, if you could look at the top column on the first page of 697. There's a heading there called "indications and usage," do you see that?

A. Yes, I do.

Q. All right. What does this tell the person who is reading this label?

A. It would tell the physician how to use Copaxone and what patient it would be indicated for.

Q. And for what conditions is Copaxone indicated?

A. Copaxone is indicated for the reduction of frequent or -- reduction of the frequency of relapses in patients with relapsing-remitting form of Multiple Sclerosis, as well as for clinically isolated syndrome with one relapse and MRI indicative of MS.

Q. Now, below that there is a section entitled dosage forms "dosage form and strength," do you see that?

A. Yes, I do.

Q. Does this tell the physician in what form Copaxone is sold?

A. It does.
Q. And in what form is it sold?
A. It's sold in prefilled syringes with one milliliter of sterile water, as well as 20 milligrams of glatiramer acetate.
Q. Now, and just above that there's a section entitled "dosage and administration," do you see that?
A. Yes, I do.
Q. And does this tell the physician how Copaxone is to be administered?
A. It does.
Q. And how is Copaxone to be administered?
A. It's to be administered with a daily injection of the prefilled syringe with the 20 milligrams of Copaxone.
Q. Now, do you know, Mr. Congleton, when Copaxone was first approved for sale in the United States?
A. Copaxone was approved in December of 1996.
Q. And do you know, sir, when Copaxone was first offered for sale in the United States by Teva?
A. Yes, I do.
Q. And when was that?
A. April 2nd of 1997.
Q. Now, in April of 1997, you were employed by Teva Neuroscience?
A. That's correct.
Q. And how large was Teva Neuroscience marketing department in

April of 1997?
A. It was two people.
Q. And who were those two people, Mr. Congleton?
A. I was the product manager, and I had a boss who was the head of our marketing department named John Asler.
Q. And was there a sales force at Teva Neuroscience at that time?
A. Yes, there was.
Q. And how large was that sales farce in April of 1997?
A. In April of 1997, we had 32 sales associates.
Q. Now, at the time that Copaxone was launched in April of 1997, were there any other MS drugs on the market?
A. Yes, there were.
Q. And what were those drugs?
A. There was Avonex as well as Betaseron, both interferons.
Q. And Copaxone is not an interferon, correct?
A. That's correct.
Q. How are interferons, just generally, Mr. Congleton, how are interferons different from Copaxone?
A. They're a different class of drugs with a different mode of action. They have common traits, but Copaxone is in a different class onto itself with a different mode of action.
Q. All right. And now you mentioned these two drugs, Avonex and Betaseron. How long had they been on the market?
A. Betaseron was launched in the United States in 1993, and

Avonex was launched in the United States in 1996.
Q. Now, are you familiar with the indicated uses for those two drugs?
A. Yes, I am.
Q. And what are they indicated for?
A. They're also indicated for the reduction of relapses in relapse-remitting Multiple sclerosis.
Q. And are you familiar with how those two drugs are to be administered?
A. Yes, I am.
Q. And how are those products administered?
A. Avonex is a once weekly intramuscular injection, and Betaseron is an every other day subcutaneous injection.
Q. Now, at the time that -- in April 1997 when Teva first started selling Copaxone, did Teva Neuroscience develop a launch plan for Copaxone?
A. Yes, we did.
Q. And could you just generally tell the court what a launch plan is?
A. A launch plan is your effort to really raise the awareness of your molecule, help physicians and patients understand how to initiate utilization of that, as well as maintain it. So it's a communication plan that introduces your product to the appropriate audiences.
Q. Were you involved in developing the launch plan for

Copaxone?
A. Yes, I was.
Q. So could you tell the Court, generally, what was that launch plan for Copaxone in April of 1997?
A. In April of 1997, it was still early in the treatment of MS, so our focus was on raising the importance of treating the disease, getting patients to begin that therapy, then to convey the benefits that Copaxone could provide patients from an efficacy and safety standpoint. We utilized our sales representatives, we utilized non-sales representative activity, such as direct mail, conventions, journal advertising.
Q. Now, you mention there were these two interferon drug products that are marketed at that time. How did Teva position itself with respect to those two interferon products?
A. Really as the non-interferon. We had a different mode of action. The efficacy we felt was comparable. A better safety tolerability standpoint due to what the experience had been with physicians with interferon. So as a different mode of action and a different clinical profile.
Q. Were there any challenges that Teva faced when it first started selling Copaxone?
A. Yes, there were.
Q. And could you just tell us, generally, what those challenges were?
A. There were several. The first would be, again MS therapies

were new to both physicians and patients, so it was the need for treating MS was a challenge.

The fact that the interferons were in the marketplace anywhere from four to about a year earlier than us, and had gained traction as an approach to treat MS. And then, frankly, the fact that we were a daily injectable versus less frequently administered medications.

Q. Do you recall, approximately, what the U.S. sales were for Copaxone in 1997?

A. Yes.

Q. And what were those sales?

A. $25 million dollars.

Q. Now, since Copaxone was launched in 1997, have other MS drugs come on to the market?

A. Yes.

Q. And what currently approved drugs does Teva consider to be competitors of Copaxone?

A. Current first line competitors would be Avonex and Betaseron, as well Extavia and Rebif, all four of those being interferons.

Q. Now, you mentioned first line treatment. What do you mean by "first line treatment"?

A. First line treatment would be a therapy that a physician would, in all likelihood, use for a newly diagnosed patient or a patient that is beginning to investigate the utilization of

therapy to manage their MS.
Q. Now, the four competitor drugs that you have identified, are those all administered by injection?
A. Yes, they are.
Q. And with what frequency are those four drugs administered?
A. The Avonex, as I've said, is a weekly intramuscular. The other interferons are either every other day or three times a week, subcutaneously.
Q. So Copaxone is still the only drug that requires administration daily?
A. That's correct.
Q. Now, just very generally, how has Teva's sales fared since it was -- its first year it was launched in 1997?
A. It's fared very well. We have, over the course of time, grown from the third entrant into the market place into the therapy of choice almost by a factor of two currently. It built over time. Copaxone has a unique profile, unique mode of action. The experience that physicians gain, they saw the benefit that their patients were deriving. As that knowledge accumulated, that experience accumulated, the utilization of Copaxone grew.

And then in 2005 with the introduction or the data from to head-to-head trials against interferons, it really continued to accelerate Copaxone's growth. Because those trials showed that Copaxone was of equal efficacacy to the

interferons, and that was contrary to the perception that was in the marketplace prior to that.

Q. Now, as part of your responsibilities with respect to the marketing and sales of Copaxone, do you keep track of patient loyalty?

A. Yes, we do.

Q. Just tell the Court, what is patient loyalty?

A. Loyalty in the context of pharmaceuticals really focuses on compliance, non-adherence. And compliance is over a given month, does patient take the drug as indicated, in Copaxone's case, are they injecting daily over those 30 days. Adherence is more of a longer term frame. It's over a given year how well the patient stayed on that therapy, so that they can derive the benefits intended.

Q. Do you know approximately what percentage of patients started on Copaxone stay with the drug?

A. Yeah, our adherence figures are approximately 85 percent at the end of the first year.

Q. Could you just give us a ballpark about how many patients are currently using Copaxone?

A. Approximately 100,000 at this point in time are benefiting from Copaxone.

Q. And as part of its services, does Teva Neuroscience offer any patients support programs with respect to Copaxone?

A. Yes, we do.

Q. Is there a name for that program?
A. Yes. It's called Shared Solutions.
Q. So, and could you describe for the Court what Shared Solutions is?
A. Shared Solutions is a free service that we offer to all people with MS.

Prior to launching the drug in 1997, we were obviously getting to know the MS marketplace, the needs of those patients. And it was clear that beyond just therapy, MS patients had emotional, psychological issues they needed to manage.

We felt it was important to create a program, our service that would help manage those barriers so the patient could go -- could be as successful as possible with the medication Copaxone. So we created the service. We made it available for all people with MS. They could have access to nurses, to educational materials. If the patient was going to begin Copaxone, then they -- a door opened to other service they had access to, such as reimbursement support, injection training, free auto-ject advice, access to the nurse, as well as other educational materials. And it has been a benefit to patients only not taking Copaxone, but obviously those taking Copaxone to help them be successful with the molecule.
Q. Patient does not have to be actually using Copaxone to have access to Teva's services?

A. That's correct.
Q. And I'm sorry, does Teva charge the patients for these services?
A. No, we do not.
Q. I'd like to just talk to you a little bit, Mr. Congleton, about the details regarding Teva's promotion of Copaxone. Could you describe for the Court what Teva's promotional strategy is for Copaxone?
A. It's really focused on, again, building the awareness of the need to treat MS, then convey the unique properties of Copaxone and the benefits that a physician's patient can derive from utilizing Copaxone to manage their Multiple sclerosis.
Q. And who is the principal audience for Teva's promotional efforts relating to Copaxone?
A. Predominantly physicians, neurologists specifically, as well as MS patients.
Q. And what methods does Teva use to promote Copaxone?
A. We utilize our sales force, as well as non-sales force activities, such as conferences, journal ads, the website, direct mail.
Q. Are you familiar with the term of "detailing"?
A. Yes, I am.
Q. Could you just explain to the court what detailing means?
A. Detailing is when our field base sales associates go into physicians' offices and talk to them about Copaxone and how it

can benefit their patients who have MS.
Q. All right. Does Teva do any direct consumer advertising such as TV ads or radio ads with respect to Copaxone?
A. No, we do not.
Q. Now, in your binder, Mr. Congleton, could you turn to the document that's labeled PTX 908? What is PTX -- 908?
A. Sorry. It's a copy of a sales aid that we would give to our sales associates.
Q. Do you know what year this document was created?
A. I believe it's 2007.
Q. And was 908 prepared under your supervision?
A. Yes, it was.
Q. And was this document prepared in the ordinary course of Teva's business?
A. Yes, it was.
MR. HASHMALL: Your Honor, plaintiffs offer PTX-908 in evidence.
MR. JONES: No objection, your Honor.
MR. DOYLE: Your Honor, Sandoz doesn't have an objection to the admission of the document for the purpose which I think it is being proffered, which is to indicate what Teva tells the MS community about Copaxone. But we do object to it being accepted for the truth of any matter asserted therein, because it's a sales aid, and there is no foundation, and there is no support for any of the actual information

contained in this document provided by this witness.

THE COURT: All right. I'll admit it.

(Plaintiff's Exhibit PTX-908 received in evidence)

MR. HASHMALL: Thank you, your Honor.

Q. And the next question, your Honor, is, for what purpose was PTX-908 created, Mr. Congleton?

A. It is the primary tool that our sales representatives utilize when detailing a physician to convey the benefits of Copaxone.

Q. And could you just tell us a bit how the sales representative uses this aid?

A. They would set up appointments with physicians, over the course of ten to 15 minute conversation use this as a supportive document to share with them data that has been published and generated on Copaxone, to talk about its efficacy, as well as safety.

Q. All right. If you could, Mr. Congleton, turn to the pages that is Bates numbers on the bottom, if you could turn to the page that has the last three digits of 909 and 910?

A. Okay.

Q. We have that up on the screen. This is a chart. What data is presented in this clarity, Mr. Congleton?

A. This is looking at the main efficacy end points that neurologists focus on when managing MS, and specifically it's looking at the effect that Copaxone has on these efficacy end

points over a sustained period of time.
Q. And so how would a salesperson at Teva use this information with the doctor when he's being, he or she is meeting with the doctor?
A. This is one of the most important points for physicians is how does your product affect the patient over the long term. So a sales representative would share with the physician what they can expect to see as a response in their patients to the use of Copaxone in managing the disease over time.
Q. And if you could, sir, turn to page with the last three digits of 912?
A. Okay.
Q. Do you have this, Mr. Congleton?
A. I do.
Q. All right. What is described on this page?
A. This is describing the pivotal trial, as well as the extended version of that trial. In this particular case it's through ten years. This is the -- one of the unique aspects about Copaxone is it is prospectively followed long term to ensure that the effect is not only immediate, but also sustained in offering benefit to a neurologist's patient.
Q. If you could turn, Mr. Congleton, to the page that has the last three digits 3915?
A. Okay.
Q. And what's described on this page, Mr. Congleton?

A. Again, this is additional efficacy information. It shows that not only is Copaxone effect sustained, but it also shows that it is immediate within the first three months you see a separation of the drug's effect to placebo.
Q. Now, does Teva train its sales staff on how to use this document, PTX-908?
A. Yes, we do.
Q. Could you turn, sir, to the document that's labeled as PTX-909 in your binder.
A. Okay.
Q. Do you recognize this document?
A. I do.
Q. And what is this document?
A. This is a sales aid training tool. It's internal use only. We provide it to our sales representatives in conjunction with the sales aid we just reviewed.
Q. And do you know what year this document was created?
A. In 2007.
Q. And was this created under your supervision?
A. Yes it was.
Q. Was this in document created in the ordinary course of Teva's business?
A. Yes, it was.
MR. HASHMALL: Your Honor, we offer PTX-909 in evidence.

MR. JONES: No objection, your Honor.
MR. DOYLE: No objection for the purpose being --
THE COURT: Purpose understanding.
MR. DOYLE: Yes, your Honor.
THE COURT: All right, admitted.
(Plaintiff's Exhibit PTX-909 received in evidence)
MR. HASHMALL: Thank you, your Honor.
Q. If you could turn to the page that's has the last three digits of 350. Could you describe what type of information is on this page, Mr. Congleton?
A. This is background information for sales associates to help them understand the graphic within that sales aid.
Q. And is this document used to instruct them in how to use the document that we had previously looked at?
A. Yes. It's a teaching aid.
Q. All right. Now on the top of that page you see there is a paragraph that's labeled direction; see that?
A. Yes, I do.
Q. What is the purpose of this paragraph?
A. It's to give the sales representative a sense for what the intents of this graphic is, the point that needs to be conveyed to the physician.
Q. All right. And then to the left on that page there is a section there entitled message musts. Do you see that?
A. Yes, I do.

Q. What are message musts?
A. There is a lot of data obviously within this graphic, and this is a way that we help the sales representative highlight what are the key points that we'd like them to convey to the physicians.
Q. Now, PTX-908 and 909, are these typical of the types of sales aids and manuals that are distributed and used by Teva sales force?
A. Yes, they are.
Q. Now, you start -- Teva Neuroscience started selling in 1997, started selling Copaxone. Has the promotional message for Copaxone changed since its introduction in 1997 until today?
A. It's evolved over time, but the core message has remained relatively constant; and that is, a unique mode of action that elicits a unique clinical profile that provides a sustained long term efficacacy in a safe and tolerable manner.
Q. Do you know what the approximate sales in the United States of Copaxone were for Teva in 2010?
A. Yes. In the United States approximately 2.25 billion.
Q. And do you know approximately how much sales have been told for Teva since introduction of the product in 1997?
A. Lifetime it's been over $10 billion.
Q. Thank you, Mr. Congleton.
MR. HASHMALL: No further questions, your Honor.

THE COURT: Cross-examination?

MR. JONES: May I begin?

THE COURT: Yes.

CROSS EXAMINATION

BY MR. JONES:

Q. Thank you, your Honor. Good morning, Mr. Congleton.

A. Good morning.

Q. Now, I think I heard, as you ended your testimony, you talked about how your sales force has stressed this unique mode of action of Copaxone; is that accurate?

A. That's correct.

Q. That's been a consistent sales strategy for Teva to talk about this unique mode of action of Copaxone; is that correct?

A. That's correct.

Q. Now, it's true, though, right, that the mechanism by which Copaxone works is not fully understood, right?

A. That's correct.

Q. In fact, no one really knows how Copaxone works, right?

A. That's correct.

Q. Now, you talked about, you talked about sales figures. Let me try and put it on a per patient level, and we can use an exhibit to help us get there.

Could I please have up 1981, PTX-1981.

Showing you, sir, if you go -- you've got a witness binder, you can look in the screen or you can look in the

witness binder, for DTX-1981. I'll represent to you and you can tell by the -- if you have the document yourself, you can see there is a Teva Bates number on it, but I'll represent to you that DTX-1981 is an excerpt from a spread sheet produced by Teva in this action. Do you recognize the information in DTX-1981, sir?

A. I do.

Q. All right. And you see that this is reported sales information as of January 5, 2010, sir?

A. Yes.

MR. JONES: All right, move admission of DTX-1981, your Honor.

MR. HASHMALL: No objection, your Honor.

THE COURT: All right, admitted.

(Defendant's Exhibit DTX-981 received in evidence)

Q. Just again, I think you talked about other methods or medications used for treating Multiple sclerosis. And we see those other medications listed on DTX 1981, correct?

A. Yes, we do.

Q. All right. And then about the one, two, three, four, the fifth medication is listed as Copaxone, correct?

A. That's correct.

Q. And if you go over to average wholesale price, we see that the average wholesale price for Copaxone is listed as $3,303, correct?

A. That's correct.
Q. So per year when you put that up per year, a patient is going to be charged $40,187 at least as of January 5, 2010, is that correct?
A. That's presuming they take 365 injections in a given year yes.
Q. And that's how it's prescribed, correct, you take a daily injection?
A. It's how it's prescribed, yes.
Q. Right. And you assumed your patients are going to be in compliance with their there medication, correct?
A. We try to help them with that, but we know the realities are they are not completely 100 percent compliant.
Q. So assuming, though, a compliant patient, a patient who wants to control their MS, which I think you'd agree most patients want to do is controlling their MS, correct?
A. That's their goal.
Q. Then they're going to be as, at least as of January 5, 2010, they're looking at $40,187 over the course of a year, correct?
A. If a hundred percent compliant, yes.
Q. Right. And that in fact when you look at the other drugs, Copaxone for yearly cost to the patient is the most expensive of the MS treatments, correct?
MR. HASHMALL: Objection, your Honor. I think the box

is obscuring the number on the bottom.

Q. Okay.

MR. HASHMALL: So I think if you --

A. It would be secondary to Tysabri.

Q. But it's certainly more expensive than Avonex, correct?

A. Yes.

Q. Betaseron, correct?

A. Yes.

Q. Extavia, correct?

A. Yes.

Q. And Rebif, right?

A. Yes.

Q. All right. Now, we've been looking at prices for January 5, 2010. Let's go to an exhibit and look to see what's happened with prices. If I could have up DTX-2022.

DTX-2022 -- and again, sir, you have that in your binder. 2022 is the SEC form 20-F, the annual report submitted by Teva Pharmaceutical for the year ended 2010. Have you ever seen form 20-F before, sir?

A. Yes I have.

Q. Right?

MR. JONES: Move admission of DTX-2022, your Honor.

MR. HASHMALL: No objection, your Honor.

THE COURT: All right, admitted.

(Defendant's Exhibit DTX-2022 received in evidence)

Q. Thank you. Just so we can have some context about Copaxone. If you go to page six. Unfortunately, this is not Bates numbered, but we'll use the organic page number of the exhibits. Page six of DTX-2022. Here we go. If you look at the 4th paragraph, it's the paragraph under the italicized portion, if I could have that blown up. Then the second sentence of that paragraph. Thank you, Nick. If I could have the second sentence of the paragraph highlighted. No, one before that. There you go. Thank you.

Now, Teva's statement to the SEC indicates that Copaxone is -- contributes disproportionately to your profits and your cash flows; is that correct?

A. It has significant impact on Teva's cash flows, yes.

Q. Well, it contributes disproportionately. That's at least what Teva told the SEC, correct?

A. That's what that does say, yes.

Q. And that's as of 2010. But in fact Copaxone has contributed disproportionately to your profits and cash flows for more than just 2010, correct?

A. It has continued to grow and add value to Teva, yes.

Q. That's right.

If we could move on in DTX-2022, if you go to page 60, 60, and if you could pull out paragraph one, two, three, fourth paragraph, the one that begins U.S. and market Copaxone sales. Thank you.

What I'm trying to get a sense, sir, is what's happened to prices. Remember we saw that spread sheet showing prices as of January 2010. We're trying to get a sense of what's happened to prices from January 2010 until present, all right. Prices have increased, correct?

A. Yes, they have.

Q. In fact according to what Teva told the SEC, you had two price increases in 2010, correct? If you look at that second sentence?

A. That's correct.

Q. Each of 9.9 percent, right?

A. That's correct.

Q. And then you had a -- so that's a total of what, about almost 20 percent sales price increase?

A. 19.8, yes.

Q. Yeah. Any reason to doubt the accuracy of that price increase reported to the SEC?

A. No, there would be no reason.

Q. Now, it also -- this discloses a second price increase that occurred I think in January 2011, if you look at the next sentence. So on top of the nearly 20 percent increase that we -- that's reported that occurred in 2010, in January 2011 you had an additional 14.9 percent increase in the sales price for Copaxone, correct?

A. That's correct.

Q. So since January of 2010, Teva has increased prices for Copaxone by about 39 percent, right?
A. That's correct. We've also seen the volume continue to grow, as well as the share grow, as it is the leading choice in treating MS.
Q. There is not much competitive pressure on you, is there
A. There's constant competitive pressure.
Q. All right, there's constant competitive pressure. Let me understand something. The rate of inflation for 2010 was about 1.5 percent, right?
A. I don't have that handy.
Q. Well, did you get any push back on raising prices by 40 percent? Did you get push back from your management saying, don't increase prices by 40 percent, inflation is only running about 1.5, push back from your management, sir?
A. We factor a lot of different things as we analyze our pricing actions.
Q. Do you agree, though, that after analyzing all those factors, including any competition that you say is out there, you agree that price has increased significantly for patients just over the course of a year, correct; 40 percent?
A. Prices have changed over time, as well as pressures within the co-pay system, the reimbursement. Lot of factors go into that, yes.
Q. Teva turn a profit on Copaxone in 2010?

A. Yes, we did.
Q. 2009 profit?
A. Yes, we did.
Q. When is the first year Copaxone became profitable for Teva?
A. I don't have that information.
Q. Well, you know about 2010, 2009. 2008, was it profitable?
A. 2008 was -- I -- honestly I focus on the U.S. portion of that, and I don't see the roll up on a global basis for Copaxone specifically.
Q. Now, you talked a little bit about marketing, and in fact you showed a label. I want to ask you some questions about the information that Teva supplies to doctors and patients in its marketing activities. Are you familiar with the term "informational marketing"?
A. Yes.
Q. Would you agree that Teva engage in informational marketing with regard to Copaxone?
A. Yes, I would.
Q. With informational marketing, what you're basically trying to do is you're doing your best to inform doctors and patients about the benefits of Copaxone, correct?
A. As well as the importance of therapy in general in managing MS.
Q. Right. So talking about the benefits, the importance of the therapy, and you're trying to give them your best

information about the risks of Copaxone, correct?
A. That's our responsibility both efficacacy and the safety of the product, yes.
Q. You take that responsibility seriously, correct?
A. Yes, we do.
Q. If you know about a risk that your product might pose to the public, you're going to tell them about it, right?
A. Within our mandate, yes.
Q. Now, starting -- you said that you've been with the -- with Copaxone since I think its launch back in 19 -- well, you said it got approval to launch in 1996 with Copaxone; is that correct?
A. Approved in '96, yes.
Q. And then but your sales were April of 1997 were first sales?
A. That's correct, in the United States.
Q. In the U.S., that's correct, sir.

Now, when you first had permission from the FDA to launch Copaxone, that was at an approved average molecular weight of 4.7 to 11 kilodalts, correct?
A. To be honest, I don't have that information right in front of me.
Q. Right. Well, let's pull up DTX-1073, then.

1073, sir, is a December 20, 1996 approval letter from the FDA to Teva; you agree?

A. Yes, I can.

MR. JONES: Move admission of DTX-1073, your Honor.

MR. HASHMALL: No objection, your Honor.

THE COURT: All right, admitted.

(Defendant's Exhibit DTX-1073 received in evidence)

Q. Thank you. If we look at DTX-1073 again, this would be the approval letter from the FDA to Teva saying that you folks had approval to market and sell Copaxone, correct?

A. That's correct.

Q. And this exhibit does have Bates numbers. If we go to TEV104078. Just look for the 78 at the bottom.

A. I'm there.

Q. Great. If you would -- thank you very much. Actually, if you just focus right on that first paragraph, great. Thank you.

So what we see here depicted on 104078 of DTX-1073 is actually the label approved by the FDA for Teva to use with Copaxone, correct?

A. That's correct.

Q. And if you look at -- this label tells us a couple of things, right? First it tells us what the average molar fraction is for Copaxone, correct?

A. It's says the average molecular weight of Copaxone, yes.

Q. Well, let's actually -- if you go right --

A. There's the fraction; yes, you're correct.

Q. Were you in the courtroom for the opening statements?
A. Yes, I was.
Q. So you have heard the discussion about molar fractions, correct?
A. I did hear.
Q. And it's your understanding, right, that Teva reports accurately it's average molar fraction when it includes that information on its Copaxone label, correct?
A. Yes.
Q. And then after that we were getting to this average molecular weight issue, if you highlight the next sentence, Nick.

This reports that Teva is authorized to sell Copaxone with an average molecular weight of 4.7 to 11 kilodaltons, correct?
A. According to the label, yes.
Q. Right. And what I've done is, I know it's 4,700 daltons, but my mouth gets tired, so I'm just going to talk about kilodaltons, you understand that 4,700 daltons is the same as 4.7 kilodaltons, right?
A. Correct. I'll refer to the dalton portion, though.
Q. Great. And, in fact, Teva went on the market when you made that first sale in April of 2007, and/or April of 1997, Teva went on the market with a Copaxone with an average molecular weight 4.7 to 11 kilodaltons, correct?

MR. HASHMALL: Objection, your Honor. What's in the label -- there was extensive testimony at the prior trial about what the manufacturing specifications and what the actually went to market with, and I don't think there is any foundation that this witness knows the answer to that question. It's going well beyond the scope of what he was testifying about on direct.

THE COURT: I can read the label. I don't know that this witness is able to testify to this.

Q. All right. Well, did you provide promotional information and labeling information to patients and doctors about the average molecular weight of Copaxone?

A. We provided prescribing information to physicians and patients, yes.

Q. Did you know the average molecular weight of Copaxone that you were selling to the public and to doctors?

A. I was aware of the label, but it's not my field of expertise. I focus on conveying the benefits of the product to physicians and patients.

Q. And you have no reason to believe that the Copaxone that you sold was outside the range of 4.7 to 11 kilodaltons, right? You have no reason to believe it was outside that average molecular weight?

A. I don't have any information about that.

Q. Okay. Now, I want to look at another label. Let's look at

Exhibit PTX-695, all right. I'm showing you PTX-695, a label for Copaxen. Go to the last page of the exhibit. You'll see that it has a revision date of January of 2002. So having looked at PTX 695, do you recognize this as a label for Copaxone as of January 2002, sir?

A. Yes.

MR. JONES: Move admission of PTX-695?

MR. HASHMALL: No objection, your Honor.

THE COURT: All right, it's admitted.

(Defendant's Exhibit PTX-695 received in evidence)

Q. Now, when we go to the first page of PTX-695, just that first paragraph -- thank you, Nick -- again we see a report and this is actually the label that patient and a doctor would see with their Copaxone that they purchased as of 2002, correct?

A. That's correct.

Q. All right. So the patient would see again these molecular fractions, right?

A. That's correct.

Q. And they would see that the average molecular weight of the product is from 4.7 to 11 kilodaltons, right?

A. That's correct.

Q. Now, and I encourage you if you need to to go ahead and look at the binder version of 695, but if you need to -- but you would you agree that in this 2002 label, regarding the 4.7 to 11 KDA Copaxone, there is no discussion about that product

being toxic in the rat basophilic leukemia in vitro assay, right?

A. No, there's not.

Q. Okay. There's no mention of 4.7 to 11 KDA Copaxone being toxic in the in vivo mouse assay, right?

MR. HASHMALL: Your Honor, I would object to this. I think, unless there is some other purpose here, I'm not able to certain -- it seems like we're going back to issues that were tried fully in July, and this is obviously the wrong witness to be questioned about this.

THE COURT: Well, I mean if there's no objection to these documents going in, you can make these arguments. I don't think we need to labor through this with this witness.

MR. JONES: And I'll get right to the point with it then.

Q. If, to your knowledge, sir, the 4.7 to level KDA Copaxone, that Teva marketed, that drug is not toxic, correct?

MR. HASHMALL: Object.

THE COURT: I'm going to sustain the objection. This is the wrong witness.

Q. Did you --

THE COURT: I like you, don't get me wrong, but you're the wrong witness on this one.

Q. Right.

THE COURT: Okay.

Q. I'll ask --

THE COURT: Let's move along, Mr. Jones.

MR. JONES: Yes, your Honor.

Q. I'll simply ask, what you told doctors and patients?

THE COURT: That's not relevant.

MR. JONES: Just so that I'm clear, your Honor, is it your preference, because I don't want to try the Court's patience on this, you're right, this is something that we can develop in argument, I do -- I was going to plan on asking him what Teva told the public in regard to toxicity for various weight ranges of Copaxone?

THE COURT: I'm assuming you can -- it's all in here. Would there be any difference in the materials that they -- what was in the label, the materials? I doubt it. I think that's your point, right?

MR. JONES: Precisely, your Honor, just simply establishing that there was no mention of toxicity to the public of 4.7 to 11 or five to nine, no mention to the public that 5 to nine was any less toxic than 4.7 to 11. That's the point.

MR. HASHMALL: Your Honor, they can argue obviously what they want from the label, but --

THE COURT: Right, I'm just trying to shorten this up.

MR. HASHMALL: I know. But I have a concern that the issue -- I don't see how this goes to any issue, other than the

issue that we tried in July, but maybe we can have that discussion later. But I'm hoping we're not going to start getting the same argument that we heard in July about differences between what they told.

THE COURT: I'm not worried right now about who is arguing what. I just want to get our witness taken care of.

MR. JONES: With that, your Honor, thank you for your guidance. I'll excuse -- thank you.

THE COURT: All right, good enough.

THE WITNESS: Thank you.

MR. DOYLE: Your Honor, I have one question. Could I just ask it from here?

THE COURT: Please, that would be great.

MR. DOYLE: Yes, your Honor.

CROSS EXAMINATION

MR. DOYLE: I'd like to know, Mr. Congleton, in any of its Copaxone marketing materials, does Teva state that the side effect profile of co-polymer-1 is associated in any way with its molecular weight?

A. With it's what? I'm sorry.

Q. Its molecular weight?

A. We share in our communications with patients beyond the efficacy and how to utilize the drug is the adverse effects that are within our product insert that are most frequent and that physicians and patients need to be aware of.

Q. My question is a little more specific, which is in its marketing materials, is there any relationship drawn by Teva between that side effect profile and molecular weight of Copaxone?

A. There is not.

MR. DOYLE: Thank you.

THE COURT: Any redirect?

MR. HASHMALL: No, your Honor.

THE COURT: All right, thank you very much. You may step down. You're excused.

We'll take a ten minute break. And who is your next witness.

MR. HASHMALL: Next witness will be Dr. Lisak.

MS. HOLLAND: Your Honor, I have the list --

(Recess)

(In open court)

THE COURT: Please be seated everybody. Call your next witness.

MR. HASHMALL: Your Honor, Mr. John Bennett is going to be putting on our next witness.

THE COURT: All right, Mr. Bennett.

MR. BENNETT: Good morning. The plaintiffs call Dr. Robert P. Lisak.

ROBERT P. LISAK,

called as a witness by the plaintiff,

having been duly sworn, testified as follows:

DIRECT EXAMINATION

BY MR. BENNETT:

THE COURT: You can be seated, sir. Thank you.

THE WITNESS: Thank you.

MR. BENNETT: Your Honor, before we begin, Dr. Lisak is our practicing physician expert, and you may remember from the pretrial conference that the parties have agreed that the practicing physician experts may appear once to accommodate their patient schedules. So Dr. Lisak is going to be providing some testimony today related to the validity issues, specifically secondary considerations of non-obviousness called long felt need and the failure of others that typically would be rebuttal testimony in this type of case.

THE COURT: All right.

MS. HOLLAND: In addition to some infringement testimony.

THE COURT: So, I'm going to hear everything I'll ever need to hear from Dr. Lisak.

MR. BENNETT: That's right.

THE COURT: That's everybody's understanding? All right, then you're wide open. Go ahead.

MR. BENNETT: Thank you.

Q. Dr. Lisak, would you please introduce yourself to the Court?

A. Robert P. Lisak.
Q. Where do you live, sir?
A. Bloomfield Hills, Michigan, which is a suburb of Detroit.
Q. Are you currently employed?
A. Yes, I am.
Q. Where are you employed, sir?
A. I'm employed at Wayne State University and the Wayne State University Physicians Group.
Q. What is your position at Wayne State, sir?
A. I'm the Chairman of Neurology and also Professor of Neurology and Professor of Immunology and Microbiology.
Q. What are your responsibilities as the Chair of Neurology and Professor at Wayne State?
A. As Chair, I'm the administrative head of the department so I'm responsible for quality issues, teaching, oversight of research finances, things like that, administrative.

As professor, I'm responsible for participating in the various teaching programs for the department.
Q. How big is the neurology department at Wayne State?
A. The full-time faculty is 35 members, but that doesn't count residents, fellows, secretaries, technicians and the laboratories, and so for the overall, probably over 100.
Q. In addition to your academic role, do you hold any other employment, sir?
A. I'm the chief of neurology at Harper University Hospital.

Q. What are your responsibilities as the chief of neurology at Harper University Hospital?
A. I'm responsible for oversight of quality of care by all of the neurologists in the department of neurology, as well oversight of the residents and fellows at the hospital, as well as administrative duties for the hospital, medical administrative.
Q. Can you give us a sense of how big the neurology practice is at Harper University Hospital?
A. We have 30 full-time neurologists in the department of neurology in the practice group, and there are another three or four private practice neurologists, plus we have 21 neurology residents, plus various fellows.
Q. Do you treat multiple sclerosis patients at Harper University Hospital?
A. Yes, we do.
Q. About how big, how many MS patients do you treat there, sir?
A. Well, the Multiple sclerosis clinic, which is run by the University Practice Group, Harper Department of Neurology, has about 3500 to 4,000 patients at any one time that we are following.
Q. Do you treat MS patients yourself?
A. Yes, I do.
Q. About how many patients do you have in your care?

A. My own personal would be about 500 patients at any one time.
Q. How long have you been treating MS patients?
A. Since 1972.
Q. Okay. Over the course of your career, about how many MS patients have you evaluated, sir?
A. Evaluated and treated, I would estimate 4500 to 5,000.
Q. Stepping back to your academic role, would you share with us what courses you teach?
A. I teach in the second year medical school student course on neurology. I teach third year students who take neurology rotation at the University Hospital. I teach fourth year students on electives, those are usually students who are thinking about a career in neurology. And then I'm also involved in teaching of the neurology residents, as well as specialty fellows, including the Multiple sclerosis fellows.
Q. Are you involved in any other type of teaching role?
A. Yes, both at Wayne State nationally and internationally I do what's called continuing medical education, CME. And that is, those are courses for already practicing physicians who wish to keep up, need to keep up in certain areas of practice. And I tend to be lecturing on multiple sclerosis and other autoimmune disease of the nervous system.
Q. Do you conduct research in your academic role?
A. Yes, I do.

Q. Has any of that research been published?
A. Yes, it has.
Q. Can you give us a sense for how much of your research has been published?
A. Peer reviewed, original observations, probably around 220 papers. Then there are reviews and chapters and editorials and so forth.
Q. Does any of this work relate to multiple sclerosis?
A. A large percentage of it does.
Q. Were you retained as an expert in this case, sir?
A. Yes, I was.
Q. Who retained you?
A. Counsel for Teva.
Q. What you were asked to do?
A. I was asked to give a brief overview of the disease multiple sclerosis and its treatments.

I was asked to give an opinion on whether Copaxone met long felt needs in the treatment of multiple sclerosis.

I was asked to give an opinion of whether there had been other attempts to find successful treatments that had failed for multiple sclerosis, and then whether I thought there were infringements on certain of the patents that I see or that are involved in this lawsuit.

Q. Thank you. In general, what are your opinions on these topics, sir?

A. I think Copaxone met a long felt need. I think there are many examples of failed therapy attempts, development therapies that failed, and that there are clear conflicts or with material that I've reviewed with related to the patents in this suit.

Q. Dr. Lisak, could you please describe your educational background for the Court?

A. Yes. I received my undergraduate degree at University of College of New York University cume laude, highest honors in history. My M.D. degree was from the College of Physicians and Surgeons of Columbia University.

Q. What did you do after you received your medical degree?

A. I did a postgraduate year, one which is commonly called internship, and I did that at Montefiore Hospital in the Bronx.

Q. What did you do after you completed your internship there?

A. I did two years of research at the National Institutes of Mental Health in Bethesda, multiple sclerosis related research.

Q. And after the NIH, what did you do next?

A. I came back and did another year of internal medicine at Bronx Municipal Hospital Center, Albert Einstein College of Medicine, and then I did a three year residency in the neurology at the hospital of the University of Pennsylvania. And during my last year I was also a trainee in allergy and immunology.

Q. Okay. When did you complete your residency at the

University of Pennsylvania?
A. End of every June of 1972.
Q. What did you do next?
A. I joined the faculty of the Department of Neurology at University of Pennsylvania, and the staff of the hospital of the University of Pennsylvania.
Q. What was your role at the hospital?
A. I was attending neurologist, and I also was the director of the multiple sclerosis clinic.
Q. How long were you the director of the MS clinic there?
A. From 1972 through 1986.
Q. Can you generally describe what your role was as the director of the clinic?
A. As director of the clinic, my role was to, in addition to seeing patients myself, was responsible for quality, for supervision of residents who rotated in the clinic, and coordination with other attending neurologists who also saw patients in the clinic.
Q. About how many patients were under your care there, sir?
A. Again about, with multiple sclerosis, about 500 at any time.
Q. Did you teach while you were at the University of Pennsylvania?
A. Yes, I did.
Q. What did you teach there?

A. I taught neurology again to 2nd, 3rd and 4th year students, neurology residents and fellows who were subspecializing in multiple sclerosis.
Q. When did you join Wayne State, sir?
A. In 1987.
Q. What position did you assume when you joined Wayne State?
A. Professor of Neurology and Chairman of the Department of Neurology, as well as I mentioned, Professor of Immunology and Microbiology.
Q. Okay. How long have you been in that position, sir?
A. I'm in my 25th year.
Q. Are you involved in any academic or medical journals from your field of work?
A. Yes, I am.
Q. Could you describe that involvement, sir?
A. I'm the editor in chief of the Journal of Neurological Sciences, which is the journal of the world federation of neurology. I'm also member of the editorial board for neuro immunology of the, of a journal called Clinical Neuropharmacology.
Q. Just briefly, when you say clinical Neuropharmacology, what does what that mean?
A. That journal publishes articles related to research in therapy of neurologic diseases.
Q. Thank you. Have you served on any other editorial boards

on in the past, sir?
A. Yes, I have.
Q. Could you describe that for us?
A. Journaled called neurology, which is the journal of the Academy of Neurology, the Anals of Neurology, Journal of Neuro Immunology, Muscle and Nerve, and the Journal of the Peripheral Nervous System.
Q. Thank you. Have you provided any lectures in the field, sir?
A. Yes, I do.
Q. Could you describe that for us?
A. I lecture, in addition to Wayne State, at other hospitals and universities, and invited talks at meetings in the United States and abroad.
Q. Have you been involved in any clinical research, sir?
A. Yes, I have.
Q. Could you describe that for us?
A. I've been involved in studies of patients with multiple sclerosis and other neurologic diseases, including clinical studies, including clinical trials.
Q. Are you involved in any professional associations?
A. Yes, I am.
Q. Could you describe that for us, sir?
A. I'm a member of the American -- I'm a fellow of the American Academy of Neurology, active now honorary member of

the American Neurologic Association, Society of Neuroscience, several others.

Q. Have you received any awards during your career?

A. Yes, I have.

Q. Could you describe those for us?

A. I was a full ride scholar in United Kingdom, I won something called a doctor's award from Myasthenia gravis foundation of America, which is given to one physician a year for clinical and/or research accomplishments. I was elected an honorary member of the American Neurologic Association, and I was elected a fellow by distinction of the Royal College of Physicians of London.

Q. Just briefly, what is Myasthenia gravis, which you --

A. Myasthenia gravis is another autoimmune disease of the nervous system. It affects where the nerve meets the muscle, so-called neuro muscular junction.

Q. Have you received any awards of late, sir?

A. Yes, I have.

Q. Could you describe that for us?

A. I just received a life time achievement award from the Consortium of Multiple Sclerosis Centers.

Q. What is the consortium of MS Centers?

A. It's an organization of centers that are involved in the treatment of patients with multiple sclerosis, as well as research with patients with multiple sclerosis.

Q. Could you give us a little more color on that, the awards that you received from the consortium, sir?
A. They give one a year to a neurologist or neuro scientist or someone involved in care or and/or research in multiple sclerosis. So I deem it a high honor.
Q. Dr. Lisak, I'd like you to turn to the tab labeled PTX-419 in your binder.
A. I have it.
Q. Do you recognize this document?
A. Yes, I do.
Q. What is it?
A. It's a copy of my, sorry, curriculum vitae, and my bibliography.
MR. BENNETT: Plaintiffs move for the admission of PTX-419, your Honor?
MS. BLOODWORTH: No objection.
THE COURT: Admitted.
(Plaintiff's Exhibit PTX-419 received in evidence)
MR. DOYLE: Your Honor, no objection as long as we're give the same opportunity with our experts.
THE COURT: I think that's probably right.
MR. DOYLE: Thank you, your Honor.
THE COURT: Okay.
MR. BENNETT: Your Honor, plaintiffs offer Dr. Lisak as an expert regarding multiple sclerosis and the treatment of

MS?

THE COURT: Any objection or voir dire requested?

MR. DOYLE: No, your Honor.

MS. BLOODWORTH: None, your Honor.

THE COURT: All right. I will accept Dr. Lisak as an expert. Go ahead.

MR. BENNETT: Thank you.

Q. Dr. Lisak, in general, what is multiple sclerosis?

A. Multiple sclerosis is an inflammatory demyelinating disease of the central nervous system, which means brain and spinal cord, and it involves inflammation affecting the brain and the spinal cord and causes demyelination.

Q. What systems within the body are involved?

A. So the central nervous system, which is considered to be the brain and the spinal cord.

Q. What systems are involved in causing the disease, sir?

A. Ah, it appears to be due to an attack by the immune system, inflammatory autoimmune cells.

Q. Okay. You mentioned that it's a demyelinating disease, right?

A. Yes, I did.

Q. What does that mean?

A. The nervous system, the actual wiring, if you will, the axons which come out of the neurons, may have an insulation around them. The insulation is a part of the tissue itself,

and it's called myelin and it serves as insulation for the actual wires, so to speak.

Q. What does the disease do to myelins, sir?

A. It destroys it.

Q. What is the practical impact of that, briefly?

A. The practical impact is that those nerves bodies that no longer have insulation do not function normally, and sometimes at all; and secondarily those, axons and neurons themselves may undergo degeneration and die and, therefore, you have permanent loss of function of those particular cells.

Q. Why is the disease called multiple sclerosis?

A. Sclerosis is because at the end of the inflammation and demyelination you get scarring. So sclerosis means scars, and multiple because there are many of them, so multiple sclerosis is the name for that reason.

Q. When was MS first recognized as a disease?

A. It was first recognized as a distinct entity back in the 1860's by a French neurologist named Sharko.

Q. Thank you. Have you helped prepare some slides that help explain the disease course associated with MS?

A. Yes, I have.

MR. BENNETT: Your Honor, with your permission I'd like Dr. Lisak to step down from the stand?

THE COURT: Sure, Doctor. Go ahead.

THE WITNESS: Thank you, your Honor. If I do this, I

think it will pick up. Thank you.

THE COURT: That should work.

THE WITNESS: Thank you.

Q. Dr. Lisak, I'm looking at slide number two. Just explain to us what we're seeing?

A. As I said, this would be a neuron, think of it is as analogy of the battery generator. This is the outgrowth of the neuron, the axon, which allows it to connect to the next neuron in the sequences. And we call this a synapse. If you look at the blown up area, this is the axon. So think of that as the platinum or the copper wire, and then think of this myelin sheet wrapped around it as the equivalent of plastic or rubber insulation, and this allows this particular axon to transmit signals to the next neuron and allows it to do it efficiently.

Q. You've got a depiction of the nervous system?

A. Yeah, this is --

Q. How does the graphic appear at top relate to that?

A. So as we're discussing multiple sclerosis, this would be the brain and the spinal cord. This would be what we would be worried about in MS, occurs in the brain and the spinal cord. Some of the rest of this is the peripheral nerves, which are not involved in multiple sclerosis. It's a central nervous system disease, brain and spinal cord.

Q. Let's move onto slide number three. And again, could you explain what we're seeing here, Dr. Lisak?

A. So what you're seeing here is cells autoimmune cells and other immune cells, inflammatory cells, get cross out of the blood into the brain and spinal cord, and for reasons that are not fully understood, they attack the myelin as if it was somebody else's myelin; thus, we use the term autoimmune disease. That leads to degeneration of the myelin, and leads to areas of the axon that are we would call bear; that is, they have no insulation. That means that at this point this axon cannot function efficiently or normally. Same would be over here. And then this is multiple of course, it's multiple sclerosis.

Q. Move to the next slide number four. And what are we looking at here?

A. Again, as I mentioned a little earlier. Now, if you look at a blowup over here, you've lost myelin, you just have some fragments. And now the bare axon not only doesn't work well, but the same inflammatory immune cells can now directly or by secreting various materials, further damage the system by damaging the axon, which is lost its myelin protection.

Q. Let's move on to the next slide number five. What do we see here?

A. And as a consequence of the lack of insulation and other factors that myelin helps the axon with, now the axon itself starts to fragment and disintegrate and die. That, therefore, means that this neuron really cannot communicate effectively

with anything that it's connected to even with the neuron that might be connecting over here. So it becomes basically non-functional and, essentially, doesn't work.

Q. And now slide number six, Dr. Lisak, what do we see here?

A. So when that happens you now have what we call dying back, so the neuron body itself, the generator of the battery dies. This cell, by not getting signal, eventually becomes dysfunctional and may die. Ultimately, the ability of the brain and spinal cord to send messages out through the peripheral nerves to the muscles and other organs and to communicate within itself is lost.

Q. Thanks. Dr. Lisak, if you like to return to the stand for a moment?

A. Yes.

Q. What happens when nerve cells die, Dr. Lisak?

A. Well, when they die, whatever function -- excuse me. Whatever function that particular nerve cell was in charge of involved with, no longer works and you get neurologic symptoms as a consequence.

Q. What are some of the practical effects of this disease course on a patient?

A. Well, it results in the patients having a lot of different neurologic symptoms at various times, severity, and if it continues to progress, you can get, and you do get permanent disability, and that leads to a patient being handicapped and

impaired, disabled.

Q. Have you prepared a slide that describes some of the symptoms and outcomes of MS?

A. Yes, I have.

Q. Let's put that up on the screen, slide number seven.

Dr. Lisak, again, describe some of these symptoms, sir?

A. These are some of the symptoms of multiple sclerosis; blurring of vision or double vision, either one, or both; loss of balance, and poor coordination; speech may become slurred; patients may develop tremors, numbness where they don't feel things well; extreme fatigue out of proportion to anything they're doing. It can affect the ability to concentrate, memory and other, what we call cognitive functions; sexual dysfunction; impaired physical mobility; dysfunction of the bladder and bowel, sometimes actual loss of ability to control the bladder or bowel, paralysis, blindness, and in a small percentage of patients, death from complications of multiple sclerosis.

Q. Is this a complete list of the symptoms?

A. No, it is not.

Q. Have you witnessed these symptoms in your own patients, sir?

A. Yes, I have.

Q. What is the impact of this disease on patient's day-to-day

life?

A. Well, it affects their ability to do many different things. So you can't read, you can't walk, you can't walk well, you can't communicate, you can't remember things, you can't feel things. Fatigue is a major problem. People who even have relatively mild physical disability can't work. They're very heat sensitive with minor changes in ambient or body temperature heat. Patients can't control their own bladder or bowel. These are major problems.

Q. When does MS typically strike?

A. The majority of patients are affected between ages 20 and 40.

Q. What is the practical impact of the disease striking at that early age?

A. Well, that's the age in which people are beginning their careers, finishing school, raising a family. So it's at the so-called peak or prime of life and development of life of an adult.

(Continued on next page)

BY MR. BENNETT:

Q. Does MS affect women and men equally, sir?

A. No, it does not.

Q. Could you explain that for us?

A. Women are affected at least three times as often as men.

Q. Do we know why that is?

A. We have theories about hormonal control of the immune system, but no single definitive answer as yet.

Q. Are there different forms of multiple sclerosis?

A. Yes, there are.

Q. What are the different forms?

A. Relapsing remitting multiple sclerosis, secondary progressive multiple sclerosis, primary progressing multiple sclerosis and the rarer form we call, for lack of a better term, progressive relapsing multiple sclerosis.

Q. If you could just briefly describe for us those different types of MS?

A. Certainly. Relapsing remitting multiple sclerosis, patients have onset over hours to days or a week or two of new neurologic symptoms referable to the brain or spinal cord which will progress for a while, then stabilize and at the beginning of the disease often improve, although not always back to baseline and with repeated episodes which may be the same symptoms or some of these other symptoms that I have on the screen, it becomes more and more deficit, there's more and more

residual damage. So that's what we call relapsing remitting multiple sclerosis.

Secondary progressive multiple sclerosis by definition is someone who had at one point relapsing remitting multiple sclerosis and now have become gradually or sometimes rapidly getting worse without any of these individual finite episodes being obviously superimposed that you can tell clinically. Primary progressive multiple sclerosis, the patients never really have relapses that we can identify, but just progress so they act like secondary progressive, yet they've never had any obvious clinical relapses.

The last form is quite rare and it's sort of, most of us treat it and I was on the committee that did this classification, consider it really a form of secondary progressive MS, but it's about less than 5 percent of the patients present with this last form.

Q. What is the most common form of the disease?

A. 85 percent of the patients with multiple sclerosis present as relapsing remitting multiple sclerosis.

Q. Briefly, what is a relapse?

A. Relapse is an appearance of new neurologic symptoms or the worsening of current symptoms or reappearance of symptoms that have cleared over a relatively short period of time that continues to worsen up to a point, then stabilizes and may or may not improve.

Q. Is there any way to predict when these relapses occur?
A. There's no definite way of predicting when they may occur.
Q. Again, what is the impact of that on a patient?
A. The impact is it's pretty difficult to live that way and to plan your life not knowing if tomorrow you might have a relapse from which you may or may not get better, how long it might last and it's at a time when people are not retired, they're in their prime of life and family, work and so forth. So it's like a hanging sword, basically.
Q. How do you diagnosis relapsing remitting MS?
A. It's based on neurologic history, neurologic examination and then we use the magnetic resonance imaging, so-called MRI, along with laboratory tests and spinal fluid in some cases to establish that it's relapsing remitting multiple sclerosis and rule out other potential diagnoses.
Q. When you perform this MRI analysis is there a particular part of the body that you focus on?
A. Yes, we focus on the brain and the spinal cord.
Q. Again, have you helped prepare a slide that explains how the MRI scan helps the diagnosis?
A. Yes, I have.
MR. BENNETT: Again, your Honor, with your permission I'd like to have Dr. Lisak stand down.
THE COURT: Sure. You may step down.
Q. Dr. Lisak, I have slide number 8, could you just explain

what we're seeing here?
A. Sure. So on this, on my left, over here, is the MRI scan of a normal, the brain of a normal individual. This is the area where the white matter, the myelin is concentrated, this is the normal spinal fluid here. That's the normal situation. On this side, I have, actually it's from a chapter of mine in a book that I edited, and you can see here that these lesions, these areas are abnormal. They're not supposed to be there, it's supposed to be clean. And these represent areas of inflammation, of demyelination and the scarring, sclerosis, so multiple sclerosis.
Q. What do those lesions do to a patient, sir?
A. These lesions, in varying combinations give you all of the symptoms. So several of these might interfere with the ability to think or process information because the circuits aren't working right. Some of these might be responsible for weakness or balance problems as an example, and this is only one cut through the brain. If you could make multiple cuts it would show many more lesions.
Q. Thanks, Dr. Lisak. Return to the stand.
Dr. Lisak, is there a cure for MS?
A. No, there is not.
Q. As a neurologist, how do you treat relapsing remitting multiple sclerosis?
A. We treat symptoms and then we administer medications, drugs

that alter the natural course of the disease, so-called disease-modifying therapies, DMT's.

Q. Briefly what is a disease-modifying therapy?

A. It's a therapy that's been shown in clinical trials that reduces some end point that is efficacious, that is something you pick as an important thing that shows that drug will modify that particular outcome in patients with multiple sclerosis.

Q. What disease-modifying therapies are currently approved by the FDA?

A. There are the so-called front line or first line, which are the interferons and Copaxone. There are the second line therapies, Novantrone and Tysabri, and there is a recently introduced oral form and I think it's too soon to say how that is going to be used.

Q. So which of these treatments do physicians typically prescribe first?

A. The first line therapies, Copaxone and the interferons.

Q. We heard a bit from Mr. Congleton about the first line therapies, but could you explain briefly what that is?

A. That's the therapies that you start with because they're proven to be efficacious. They have a reasonable side effect profile; some toxicities for some of them but nothing usually life-threatening, and they are reasonably well tolerated by the patients, so that would be a first line, front line therapy.

Q. Are there second line treatments?

A. Yes, as I mentioned, there are.
Q. What is a second line treatment?
A. Second line is also, it could be, is a drug or a treatment that's effective, is safe enough that it was approved by the FDA, but some of those tolerability and especially safety issues are such that you wouldn't start, most people would not start with those first. They would see if a patient responded to one of the first line therapies for at least for a while.
Q. Okay. Now, you mentioned a drug being effective, but what do you mean when you say the word "effective"?
A. Well, there's a few definitions. One would be in a clinical trial and that's what the FDA takes, so going forward as I understand it, you tell the FDA what you think the end points would be; reduction of the relapses, less disability, whatever you think are important, you pick important ones that you and the FDA agree on and that would be efficacious.

As a physician practicing, it's also what you see in your own practice, that is, patients who were put on the medications seem to be doing well, better than they've been doing before they were put on the medication. That would be as a practical physician's mind, so they overlap a little bit, but the latter is not as clearly defined as the FDA's.
Q. You also mentioned safety and tolerability. Could you explain what you mean by those terms?
A. Safety means does the drug in question for MS or any other